PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference P813PC00	**FOR FURTHER ACTION**	See Form PCT/IPEA/416
International application No. PCT/DK2004/000695	International filing date *(day/month/year)* 11.10.2004	Priority date *(day/month/year)* 10.10.2003
International Patent Classification (IPC) or national classification and IPC A61K7/06		
Applicant COSMEDICAL APS et al		

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 6 sheets, including this cover sheet.
3. This report is also accompanied by ANNEXES, comprising:
   a. ☒ *sent to the applicant and to the International Bureau)* a total of 13 sheets, as follows:
      ☒ sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).
      ☐ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.
   b. ☐ *(sent to the International Bureau only)* a total of (indicate type and number of electronic carrier(s)) , containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).

4. This report contains indications relating to the following items:
   - ☒ Box No. I Basis of the opinion
   - ☐ Box No. II Priority
   - ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - ☐ Box No. IV Lack of unity of invention
   - ☒ Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - ☐ Box No. VI Certain documents cited
   - ☐ Box No. VII Certain defects in the international application
   - ☐ Box No. VIII Certain observations on the international application

Date of submission of the demand	Date of completion of this report
14.06.2005	19.12.2005
Name and mailing address of the international preliminary examining authority: European Patent Office - P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk - Pays Bas Tel. +31 70 340 - 2040 Tx: 31 651 epo nl Fax: +31 70 340 - 3016	Authorized Officer Fischer, J.P. Telephone No. +31 70 340-2440

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
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Box No. I Basis of the report

1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.

   ☐ This report is based on translations from the original language into the following language , which is the language of a translation furnished for the purposes of:
   - ☐ international search (under Rules 12.3 and 23.1(b))
   - ☐ publication of the international application (under Rule 12.4)
   - ☐ international preliminary examination (under Rules 55.2 and/or 55.3)

2. With regard to the **elements*** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

Description, Pages

1-23	as originally filed

Claims, Numbers

82-86	as originally filed
1-81	received on 14.06.2005 with letter of 14.06.2005

Drawings, Sheets

1-6	as originally filed

☐ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing

3. ☒ The amendments have resulted in the cancellation of:
   - ☐ the description, pages
   - ☒ the claims, Nos. 82-86
   - ☐ the drawings, sheets/figs
   - ☐ the sequence listing *(specify)*:
   - ☐ any table(s) related to sequence listing *(specify)*:

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).
   - ☐ the description, pages
   - ☐ the claims, Nos.
   - ☐ the drawings, sheets/figs
   - ☐ the sequence listing *(specify)*:
   - ☐ any table(s) related to sequence listing *(specify)*:

* *If item 4 applies, some or all of these sheets may be marked "superseded."*

Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-81
	No:	Claims	
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-20,23-24,41,45-61,64-70,76-77
Industrial applicability (IA)	Yes:	Claims	1-81
	No:	Claims	

2. Citations and explanations (Rule 70.7):

see separate sheet

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

The following documents D7 and D8 were cited in the international search report.
D7: EP-A-0 622 069 (PROTOPAPA EVANGELIA ; SEKERIS CONSTANTINE E (GR)) 2 November 1994 (1994-11-02)
D8: WO 98/02134 A (JOHNSON & JOHNSON CONSUMER PRODUCTS) 22 January 1988 (1998-01-98)

1. The amendments filed with the letter dated 14.06.2005 do not introduce subject-matter which extends beyond the content of the application as originally filed, in accordance with Article 34(2)(b)PCT.

2. Original claims 45, 47 and 71 have been amended (respect. new claims 45, 47 and 66) by specifying the type of enzymes to be used in the composition and by a limitation to the water activity reducing agent.

3. The amended claims 45 and 47 are novel in view of D1, D4, D5 and D6 . None of D1, D4, D5 and D6 disclose compositions containing the specified enzymes in combination with at least 92 % weight of a water activity reducing agent and a solvent.

4. The amended claim 66 is new in view of D3 for the limitation of the water activity reducing agent.

5. The use of proteolytic enzymes as active agents against unwanted hair growth is already known by the skilled person, see for example the applicant knowledge (page 2, lines 19-21) or D7 which discloses the use of compositions containing papain or chymotrypsin as permanent enzymatic depilation compositions and D8 which discloses the use of enzymes like serine proteases as hair growth inhibitor.

The problem solved by the present application is the preparation of a hair growth inhibitor composition containing proteolytic enzymes as active agents with increased storage stability.

The enzyme stability problem is a problem well known in the state of the art, D1 solves indeed the problem of making a better stabilized enzymatic composition by adding up to 99,99 % by weight of a polyol as a water activity reducing agent to a composition comprising an active agent, for example a protease enzyme and a solvent .

Thus a skilled person would regard as a normal option to use an enzymatic cosmetic composition with improved stability as disclosed in D1.

Therefore claims 1-20,23-24 and 41 do not meet the requirements of the PCT in respect of inventive step (Article 33(3)PCT).

6. Using specified protease enzymes like trypsin, chymotrypsin, papain or bromelain (claims 45 and 47) is an obvious alternative to the enzymes used in D1, all the more since they are commonly used in cosmetic compositions against unwanted hair growth and since their stabilization with high proportions of polyols as water activity reducing agents has been described in D6.

Therefore claims 45-61 and 64-65 do not meet the requirement of the PCT in respect of inventive step (Article 33(3)PCT).

7. The use of a two-part dispensing system (claim 66) does not involve an inventive step in view of D3 which describes a two-parts dispensing system containing as a first composition an aqueous enzyme composition stabilized by a high concentration of water activity reducing agent (up to 90 %). The stabilized enzyme can be any enzyme of interest (column 6, lines 57-63) like protease enzymes (serine protease powder as in example 1 or cysteine protease powder like papain as in example 3).

Therefore claims 66-70 and 76-77 do not meet the requirement of the PCT in respect of inventive step (Article 33(3)PCT).

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8. Industrial applicability

The subject-matter of claims 1-81 is considered industrially applicable and therefore claims 1-81 do meet the requirements of Article 33(4)PCT.

9. Minor objections

Claims 67-81 are dependant from the new amended claim 66 and not from 71.

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Amended Claims

1. Use of a composition comprising
at least one enzyme, said enzyme being dissolved in a solvent, and

water activity reducing agent, wherein said water activity reducing agent constitutes at least 50 percent by weight of the composition
for the preparation of a hair growth inhibitor.

2. The use of the composition according to claim 1, wherein the at least one enzyme is a proteolytic enzyme.

3. The use of the composition according to claim 1, wherein the at least one enzyme is an enzyme selected from the group of enzymes consisting of trypsin, chymotrypsin, papain, bromelain.

4. The use of the composition according to claim 1, wherein wherein the at least one enzyme is an enzyme selected from the group of enzymes consisting of trypsin and chymotrypsin.

5. The use of the composition according to claim 1, wherein the at least one enzyme is trypsin.

6. The use of the composition according to claim 1, wherein the solvent is water.

7. The use of the composition according to any of the preceding claims, wherein the water activity reducing agent is selected from glycerine, sorbitol, saccharose, saline.

8. The use of the composition according to claim 7, wherein the water activity reducing agent is glycerine.

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9. The use of the composition according to any of the preceding claims, wherein the water activity reducing agent constitutes at least 60 percent by weight of the composition, such as at least 70 percent by weight of the

composition, at least 80 percent by weight of the composition at least 85 percent by weight of the composition, at least 90 percent by weight of the composition, at least 92 percent by weight of the composition, at least 95 percent by weight of the composition, at least 98 percent by weight of the composition.

10. The use of the composition according to claim 1, said composition further comprising a polymer.

11. The use of the composition according to claim 1, wherein the polymer cross-binds the solvent in the composition.

12. The use of the composition according to claim 11, wherein the polymer comprises acrylic acid monomers.

13. The use of the composition according to claim 11 or 12, wherein the polymer is an acrylic acid polymer.

14. The use of the composition according to claim 1, wherein the polymer is selected from carboxymethylene resins, polyacrylic acid, C10-C30 alkyl propenoate, polymer with propenoic acid, butenoic acid and/or alkyl propenoates, products with propenyl sucrose ether or propenyl 2,2-dihydroxymethyl-1,3-propanediol.

15. The use of the composition according to claim 1, wherein the solvent and the enzyme constitutes at the most 20 percent by weight of the composition.

16. The use of the composition according to claim 1, wherein the solvent and the enzyme constitutes at the most 15 percent by weight of the composition, such as at the most 10 percent by weight of the composition, such as at the most 5 percent by weight of the composition.

17. The use of the composition according to claim 1, wherein the polymer constitutes 0.2 percent by weight of the composition.

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18. The use of the composition according to any of the preceding claims, wherein the polymer constitutes at most 1.5 percent by weight of the composition, such as at most 1 percent by weight of the composition, at most 0.5 percent by weight of the composition at most 0.3 percent by weight of the composition, at most 0.275 percent by weight of the composition, at most 0.25 percent by weight of the composition, at most 0.2 percent by weight of the composition.

19. The use of the composition according to claim 1, wherein the enzyme (200 F.I.P-U/g) constitutes 2.5 percent by weight of the composition.

20. The use of the composition according to any of the preceding claims, wherein the enzyme constitutes at least 7.5 percent by weight of the composition, such as at least 6 percent by weight of the composition, at least 5 percent by weight of the composition at least 4 percent by weight of the composition, at least 3 percent by weight of the composition, at least 2.75 percent by weight of the composition, at least 2.5 percent by weight of the composition.

21. The use of the composition according to any of claims 10-18, said composition further comprising an agent capable of neutralising the polymer.

22. The use of the composition according to claim 21, wherein the agent is diisopropanolamin.

23. The use of the composition according to any of the preceding claims, wherein the composition is in the form of a creme, a paste, a gel or a liquid.

24. The use of the composition according to any of the preceding claims, wherein the composition is in the form of a creme, a gel or a paste.

25. Use of a system comprising

A first component comprising

a first composition comprising

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at least one enzyme, said enzyme being dissolved in a solvent, and

a water activity reducing agent

a second component comprising

a second composition, comprising

at least one enzyme-activating agent and/or

at least one anti-inflammatory, penetration-promoting agent and/or

a preservative agent

for the preparation of a hair growth inhibitor.

26. The use of the system according to claim 25, wherein the first composition is defined in any of the claims 1-24.

27. The use of the system according to claim 25, wherein the two compositions of the two components of the system are in separate compartments.

28. The use of the system according to claim 25, wherein the second composition of the second component of the system comprises the at least one enzyme-activating agent consisting essentially of a solvent.

29. The use of the system according to claim 25, wherein the second composition of the second component of the system comprises the at least one enzyme-activating agent consisting essentially of water.

30. The use of the system according to claim 25, wherein the second composition of the second component of the system further comprises at least one penetration-promoting, anti-inflammatory agent.

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31. The use of the system according to claim 25, wherein the second composition of the second component of the system further comprises the at least one penetration-promoting, anti-inflammatory agent selected from a group of salicylates.

32. The use of the system according to claim 25, wherein the second composition of the second component of the system further comprises diethylamine salicylate.

33. The use of the system according to claim 25, wherein the second composition of the second component of the system further comprises at least one preservative agent.

34. The use of the system according to claim 25, wherein the at least one preservative agent of the second composition of the second component of the system is sodium benzoate.

35. The use of the system according to any of the claims 25-34, wherein the at least one enzyme-activating agent of the second composition of the second component of the system constitutes 95 percent by weight of the second component.

36. The use of the system according to any of the claims 26-34, wherein the at least one enzyme-activating agent of the second composition of the second component of the system constitutes 90 percent by weight of said second composition of the second component of the system, such as at least 80 percent by weight of said second composition of the second component, such as at least 70 percent by weight of said second composition of the second component of the system, such as at least 60 percent by weight of said second composition of the second component of the system, such as at least 50 percent by weight of said second composition of the second component of the system, such as at least 40 percent by weight of said second composition of the second component of the system, such as at least 30 percent by weight of said second composition of the second component

of the system, such as at least 30 percent by weight of said second composition of the second component of the system.

37. The use of the system according to any of the claims 25-34, wherein the at least one penetration-promoting, anti-inflammatory agent of the second composition of the second component of the system constitutes 2 percent by weight of said second composition of the second component of the system.

38. The use of the system according to any of the claims 25-34, wherein the at least one penetration-promoting, anti-inflammatory agent of the second composition of the second component of the system constitutes 3 percent by weight of said second composition of the second component of the system, such as at least 4 percent by weight of said second composition of the second component of the system, such as at least 5 percent by weight of said second composition of the second component of the system.

39. The use of the system according to any of the claims 25-38, wherein the at least one preservative agent of the second composition of the second component of the system constitutes 1 percent by weight of said second composition of the second component of the system.

40. The use of the system according to any of the claims 25-38, wherein the at least one preservative agent of the second composition of the second component of the system constitutes 0.8 percent by weight of said second composition of the second component of the system, such as at least 0.5 percent by weight of said second composition of the second component of the system, such as at least 0.3 percent by weight of said second composition of the second component of the system, such as at least 0.1 percent by weight of said second composition of the second component of the system.

41. A method for inhibiting hair growth, said method comprising the steps of

a. applying the composition as defined in claims 2-24 or the first composition of a system as defined in claims 25-40 to the body parts having accessible hair follicles

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b. allowing said composition to access at least part of the accessible hair follicles thereby inhibiting hair growth.

42. The method according to claim 41 further comprising a step for

a. applying the second composition of the second component of the system as defined in any of the claims 25-40 subsequent to application of the composition as defined in claims 1-24 or the first composition of the first component of the system as defined in claims 25– 40.

43. The method according to claims 41 and 42, wherein the composition as defined in claims 1-24 or the composition of the first component of the system as defined in claims 25-40 is allowed to access the accessible hair follicles for a period in the range of 1- 20 min.

44. The method according to claim 42, wherein the second composition of the second component of the system as defined in claims 25-40 further is allowed to access the accessible hair follicles for a period in the range of 5-6 hrs subsequent to the application of the first composition of the first component of the system as defined in claims 25 and 26 or the composition as defined in claims 1-24.

45. A method for the preparation of a hair growth inhibitor

a. providing at least one enzyme selected from the group of enzymes consisting of trypsin, chymotrypsin, papain bromelain, at least one solvent, and at least one water activity reducing agent, and

b. mixing the at least one enzyme, the at least one solvent, and the at least one water activity reducing agent in a manner such that the water activity reducing agent constitutes at least 92 percent weight of the hair growth inhibitor.

46. The method according to claim 45, wherein the at least one enzyme, the at least one solvent, and the at least one water activity reducing agent are as defined in any of the claims 1-24.

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47. A composition for inhibiting hair growth comprising

at least one enzyme selected from the group of enzymes consisting of trypsin, chymotrypsin, papain bromelain, said enzyme being dissolved in a solvent, and

water activity reducing agent, wherein said water activity reducing agent constitutes at least 92 percent by weight of the composition.

48. The composition according to claim 47, wherein the solvent is water.

49. The composition according to any of the preceding claims, wherein the water activity reducing agent is selected from glycerine, sorbitol, saccharose, saline.

50. The composition according to claim 7, wherein the water activity reducing agent is glycerine.

51. The composition according to claim 47, said composition further comprising a polymer.

52. The composition according to claim 47, wherein the polymer cross-binds the solvent in the composition.

53. The composition according to claim 57, wherein the polymer comprises acrylic acid monomers.

54. The composition according to claim 57 or 58, wherein the polymer is an acrylic acid polymer.

55. The composition according to claim 47, wherein the polymer is selected from carboxymethylene resins, polyacrylic acid, C10-C30 alkyl propenoate, polymer with propenoic acid, butenoic acid and/or alkyl propenoates,

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products with propenyl sucrose ether or propenyl 2,2-dihydroxymethyl-1,3-propanediol.

56. The composition according to claim 1, wherein the solvent and the enzyme constitutes at the most 20 percent by weight of the composition.

57. The composition according to claim 47, wherein the solvent and the enzyme constitutes at the most 15 percent by weight of the composition, such as at the most 10 percent by weight of the composition, such as at the most 5 percent by weight of the composition.

58. The composition according to claim 47, wherein the polymer constitutes 0.2 percent by weight of the composition.

59. The composition according to any of the preceding claims, wherein the polymer constitutes at most 1.5 percent by weight of the composition, such as at most 1 percent by weight of the composition, at most 0.6 percent by weight of the composition at most 0.3 percent by weight of the composition, at most 0.275 percent by weight of the composition, at most 0.25 percent by weight of the composition, at most 0.2 percent by weight of the composition.

60. The composition according to claim 47, wherein the enzyme (200 F.I.P-U/g) constitutes 2.5 percent by weight of the composition.

61. The composition according to any of the preceding claims, wherein the enzyme constitutes at least 7.5 percent by weight of the composition, such as at least 6 percent by weight of the composition, at least 5 percent by weight of the composition at least 4 percent by weight of the composition, at least 3 percent by weight of the composition, at least 2.75 percent by weight of the composition, at least 2.5 percent by weight of the composition.

62. The composition according to any of claims 47-66, said composition further comprising an agent capable of neutralising the polymer.

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63. The composition according to claim 67, wherein the agent is diisopropanolamin.

64. The composition according to any of the preceding claims, wherein the composition is in the form of a creme, a paste, a gel or a liquid.

65. The composition according to any of the preceding claims, wherein the composition is in the form of a creme, a gel or a paste.

66. A system for inhibiting hair growth comprising

A first component comprising
a first composition comprising

at least one enzyme selected from the group of enzymes consisting of trypsin, chymotrypsin, papain bromelain, said enzyme being dissolved in a solvent, and

a water activity reducing agent constituting at least 92 percent by weight of the composition

a second component comprising
a second composition, comprising
at least one enzyme-activating agent and/or

at least one anti-inflammatory, penetration-promoting agent and/or

a preservative agent.

67. The system according to claim 71, wherein the first composition is defined in any of the claims 48-70.

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68. The system according to claim 71, wherein the two compositions of the two components of the system are in separate compartments.

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69. The system according to claim 71, wherein the second composition of the second component of the system comprises the at least one enzyme-activating agent consisting essentially of a solvent.

70. The system according to claim 71, wherein the second composition of the second component of the system comprises the at least one enzyme-activating agent consisting essentially of water.

71. The system according to claim 71, wherein the second composition of the second component of the system further comprises at least one penetration-promoting, anti-inflammatory agent.

72. The system according to claim 71, wherein the second composition of the second component of the system further comprises the at least one penetration-promoting, anti-inflammatory agent selected from a group of salicylates.

73. The system according to claim 71, wherein the second composition of the second component of the system further comprises diethylamine salicylate.

74. The system according to claim 71, wherein the second composition of the second component of the system further comprises at least one preservative agent.

75. The system according to claim 71, wherein the at least one preservative agent of the second composition of the second component of the system is sodium benzoate.

76. The system according to any of the claims 71-80, wherein the at least one enzyme-activating agent of the second composition of the second component of the system constitutes 95 percent by weight of the second component.

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77. The system according to any of the claims 71-80, wherein the at least one enzyme-activating agent of the second composition of the second component of the system constitutes 90 percent by weight of said second composition of the second component of the system, such as at least 80 percent by weight of said second composition of the second component, such as at least 70 percent by weight of said second composition of the second component of the system, such as at least 60 percent by weight of said second composition of the second component of the system, such as at least 50 percent by weight of said second composition of the second component of the system, such as at least 40 percent by weight of said second composition of the second component of the system, such as at least 30 percent by weight of said second composition of the second component of the system, such as at least 30 percent by weight of said second composition of the second component of the system.

78. The system according to any of the claims 71-80, wherein the at least one penetration-promoting, anti-inflammatory agent of the second composition of the second component of the system constitutes 2 percent by weight of said second composition of the second component of the system.

79. The system according to any of the claims 71-80, wherein the at least one penetration-promoting, anti-inflammatory agent of the second composition of the second component of the system constitutes 3 percent by weight of said second composition of the second component of the system, such as at least 4 percent by weight of said second composition of the second component of the system, such as at least 5 percent by weight of said second composition of the second component of the system.

80. The system according to any of the claims 71-84, wherein the at least one preservative agent of the second composition of the second component of the system constitutes 1 percent by weight of said second composition of the second component of the system.

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81. The system according to any of the claims 71-84, wherein the at least one preservative agent of the second composition of the second component of

the system constitutes 0.8 percent by weight of said second composition of the second component of the system, such as at least 0.5 percent by weight of said second composition of the second component of the system, such as at least 0.3 percent by weight of said second composition of the second component of the system, such as at least 0.1 percent by weight of said second composition of the second component of the system.

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